Appendix 2

Non-technical Abstract

Melanoma is a disease of the skin in which cancer cells are found in the cells that color the skin, called melanocytes. Melanoma is associated with exposure to the sun, and is 40 times more prevalent in whites than blacks. It is far more serious than other types of skin cancer, accounting for three-quarters of all deaths from skin cancer despite representing only 5% of all skin cancer cases. Because chemotherapy has relatively little impact on the natural history of metastatic melanoma, researchers are looking to other therapies as possible approaches to melanoma treatment.

This clinical investigation uses a vaccine in an effort to stimulate the patient's immune system into destroying cancerous cells. The word vaccine as used here may be different from the conventional meaning of the word. Whereas prophylactic vaccines have been administered to prevent the onset of disease, the term vaccine as used here refers to an investigational therapeutic treatment designed to bolster the anti-tumor cell immune response in patients already diagnosed with a particular disease, like melanoma. Tumor vaccines are also known as cancer immunotherapy.

This clinical investigation employs the use of two adenovirus vectors, Ad2/MART-1v2 and Ad2/gp100v2, which separately contain the blueprint for one of two human melanoma tumor proteins, Melan-A/MART-1 or gp100. These proteins act as markers on cancer cells, enabling the body's T lymphocytes to recognize the cancerous cells and possibly destroy them. The adenovirus vectors work as a vehicle to carry the blueprint for the melanoma proteins into the body. The adenovirus used in this study is a common virus that can infect human airways, resulting in respiratory and cold or flu-like symptoms. However, it has been genetically altered so that it cannot reproduce and cause illness.

Earlier generations of these adenovirus vectors have been used previously in human clinical trials and have proved to be well-tolerated. Also, these second-generation adenovirus vectors containing the blueprint for either Melan-A/MART-1 or gp100 currently are being tested in another Genzyme-sponsored human clinical trial and have thus far proved to be well-tolerated.

This Phase I/II, open label trial will evaluate the safety and immunogenicity of the Ad2/MART-1v2 and Ad2/gp100v2 adenoviruses. Patients with stage II, III, and IV malignant melanoma who have had their melanoma surgically removed will be sequentially enrolled into one of three groups (each group evaluating a higher dose than the last) to receive up to 6 vaccinations by intradermal (ID) administration with 21 days (3 weeks) between each vaccination. Study subjects will receive Ad2/MART-1v2 or Ad2/gp100v2 sequentially, or both vectors concurrently, at one of three dose levels. Thirty-nine patients have been enrolled in this study.

Once the product is delivered to the body, the goal of the vaccine is to stimulate the immune system to seek out and attack cancerous cells. The general safety of these adenoviral vectors and their ability to elicit an immune response have been demonstrated in extensive pre-clinical animal and cell culture studies and in several human clinical trials.